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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/786,072 | 03/14/2001 | Thomas Koehler | WEH204 | 6854 |

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| EXAMINER | |
|---|---|
| STRZELECKA, TERESA E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | 22 |

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/786,072 | KOEHLER, THOMAS | |
| | Examiner | Art Unit | |
| | Teresa E Strzelecka | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *April 21, July 15, and September 5, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 5, 2003 has been entered.

2. Applicant's amendment filed July 15, 2003 has been entered. The amendment overcame the following: objections to claims 1, 6, 14, 17, 25, 28 and 29 and rejection of claims 1-29 under 35 U.S.C. 112, second paragraph. Rejection of claims 1-5 and 29 under 35 U.S.C. 102(b) over Day et al. is maintained for reasons given in the "Response to Arguments" section.

3. Claims 1-34 are pending and will be considered.

### *Response to Arguments*

4. Applicant's arguments filed July 15, 2003 have been fully considered but they are not persuasive.

Regarding rejection of claims 1-5 and 29 under 35 U.S.C. 102(b) over Day et al., Applicants argues that addition of a limitation "which reaction chambers are storable without problems for a prolonged period of time with unchanged quality" to claim 1 and addition of a limitation "wherein the reaction chamber is suitable to be stored at room temperature for a period longer than a year without loss of quality" to claim 29 overcome the rejection, since the plates of Day et al. withstand the conditions of postal transport.

The new limitations are not structural limitations, i.e., they do not introduce any characteristics into the product which distinguishes the product from the prior art. Also, since the

plates of Day et al. contain the same elements as the claimed reaction chambers of the instant application, they are expected to exhibit the same properties, namely, to be storable without problems for prolonged periods of time and to be storable at room temperature.

The rejection is maintained.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite because of the limitation "serve for producing a thinning sequence out of the calibrated nucleic acid". It is not clear what it means to "produce a thinning sequence out of nucleic acid".

***Claim Interpretation***

7. The term "reaction chamber" is interpreted as any container.

8. The terms "calibrated nucleic acid", "carrier nucleic acid" and "standard nucleic acid" are interpreted as any nucleic acid, since they were not defined in the specification.

9. The following rejection is based on the product claimed in claims 1, 29 and 30, which is "Reaction chambers coated with native, synthetically or enzymatically prepared nucleic acids", irrespective of the way in which they were obtianed (see MPEP 2113 and 2114). Further, the limitations "storable without problems for a prolonged period of time with unchanged quality" (claim 1) and "suitable to be stored at room temperature for a period longer than a year without loss of quality" (claim 29) refer to the properties of the reaction chambers, not their structural

limitations. The limitations "useable for kits" (claim 2), use of dilution solutions (claims 4 and 33) are intended use limitations, which, again, do not impose structural constraints on the product (see MPEP 2114).

## MPEP 2113 Product-by-Process Claims

PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

**MPEP-2114 [R-1] Apparatus and Article Claims — Functional Language**

APPARATUS CLAIMS MUST BE STRUCTURALLY DISTINGUISHABLE FROM THE PRIOR ART

>While features of an apparatus may be recited either structurally or functionally, claims< directed to >an< apparatus must be distinguished from the prior art in terms of structure rather than function. >In re Schreiber, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997) (The absence of a disclosure in a prior art reference relating to function did not defeat the Board's finding of anticipation of claimed apparatus because the limitations at issue were found to be inherent in the prior art reference); see also In re Swinehart, 439 F.2d 210, 212-13, 169 USPQ 226, 228-29 (CCPA 1971);< In re Danly, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA 1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990) (emphasis in original).

MANNER OF OPERATING THE DEVICE DOES NOT DIFFERENTIATE APPARATUS CLAIM FROM THE PRIOR ART

A claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. Ex parte Masham, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987)

**MPEP 2114.**

**MANNER OF OPERATING THE DEVICE DOES NOT DIFFERENTIATE APPARATUS CLAIM FROM THE PRIOR ART**

A claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. Ex parte Masham, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987) (The preamble of claim 1 recited that the apparatus was "for mixing flowing developer material" and the body of the claim recited "means for mixing ..., said mixing means being stationary and completely submerged in the developer material". The claim was rejected over a reference which taught all the structural limitations of the claim for the intended use of mixing flowing developer. However, the mixer was only partially submerged in the developer material. The Board held that the amount of submersion is immaterial to the structure of the mixer and thus the claim was properly rejected.).

***Claim Rejections - 35 USC § 102***

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-4, 29 and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Day et al. (Biotechniques, vol. 18, pp. 981-984, 1995; cited in the previous office action).

Day et al. teach 96-well plates coated with DNA templates which were dried in the wells. The plates can then be used for setting up PCR reactions. Alternatively, PCR primers are distributed into the wells and dried there. In both cases, adherence of the dried DNA to the walls of the wells is non-covalent, since both dried template and dried primers function in subsequent PCR reactions (page 381-383).

11. Claims 1, 3, 4, 6, 8, 11, 14, 15, 17, 19, 22, 25, 26, 29, 30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Klatser et al. (J. Clin. Microbiol., vol. 36, pp. 1798-1800, June 1998).

Regarding claims 1, 3, 4, 29, 30, 32 and 33, Klatser et al. teach containers with DNA primers which were non-covalently adsorbed onto the surface by freeze-drying (page 1798, third paragraph; page 1799, second paragraph).

Regarding claims 6 and 17, Klatser et al. teach a method for the production of reaction chambers, the method comprising

directly aliquoting calibrated standard nucleic acids and added carrier nucleic acid into reaction chambers and subsequently non-covalently adsorbing the calibrated standard nucleic acids and added carrier nucleic acids directly in the inner wall of the reaction chamber by means of freeze-drying or vacuum-centrifugating lyophilization (Klatser et al. teach directly adsorbing DNA primers onto container walls by lyophilization of batches of PCR mixes, comprising PCR primers (page 1798, third paragraph). Klatser et al. do not specifically teach a container, but since the samples were lyophilized, they had to be placed in a container, therefore, inherently, Klatser et al. teach the limitations of these claims).).

Regarding claims 8 and 19, Klatser et al. teach using DNA primers (page 1798, third paragraph).

Regarding claims 11 and 22, Klatser et al. teach primers for detection of two different Mycobacterium tuberculosis genes, IS6110 and 16S rRNA (page 1798, second paragraph).

Regarding claims 14 and 25, Klatser et al. teach lyophilizating PCR reaction mix comprising primers, DNA polymerase, dNTPs and uracil-DNA-glycosylase (page 1798, third paragraph).

Regarding claims 14, 15 and 25, Klatser et al. teach forming a kit for the detection of Mycobacterium tuberculosis (page 1799, second paragraph).

***Claim Rejections - 35 USC § 103***

12. Claims 5 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Day et al. (Biotechniques, vol. 18, pp. 981-984, 1995; cited in the previous office action), Koehler et al. (Biotechniques, vol. 23, pp. 722-726, 1997; cited in the IDS) and Barany et al. (U.S. patent No. 5,494,810).

A) Day et al. do not teach carrier nucleic acid being λ DNA.

B) Koehler et al. teach addition of λ DNA digested with HindIII as a carrier to stabilize standard DNA in solution (page 724, second paragraph; page 725, second paragraph). Koehler et al. do not teach sonicated λ DNA.

C) Barany et al. teach using sonicated salmon sperm DNA as a carrier (col. 34, lines 29, 30).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used λ DNA as a carrier in the formation of plates of Day et al. The motivation to do so, provided by Koehler et al., would have been that presence of carrier DNA stabilized DNA in dilute solution and prevented non-specific binding of DNA to the tubes (page 724, second paragraph) and diminished variability in the amplification reactions using the competitor in solution (page 725, second paragraph). The motivation to sonicate the λ DNA of Koehler et al., provided by Barany et al., would have been that the sonicated DNA provided no background in amplification reactions (col. 36, lines 21-23).

13. Claims 2, 7, 12, 13, 16, 18, 23, 24, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klatser et al. (J. Clin. Microbiol., vol. 36, pp. 1798-1800, June 1998), Cottingham

(U.S. Patent No. 5,948,673), Irvine et al. (U.S. Patent No. 6,300,056) and Longiaru et al. (EP 0 420 260 A2).

A) Klatser et al. teach lyophilization of PCR reaction mixes, but do not specifically teach plastic or glass containers, 96 reaction chambers or different concentrations of aliquoted nucleic acids.

B) Regarding claims 2, 7 and 18, Cottingham teaches a DNA card comprising dried nucleic acid amplification reagents in the wells of sample chambers which are formed from plastic (col. 3, lines 45-48; col. 7, lines 55-64).

Regarding claims 12, 16, 23, 27 and 28, Cottingham teaches a DNA card comprising 64 identical sample cells, arranged in eigth rows and eight columns (col. 6, lines 19-25). The wells are sealed with a flexible, pressure sensitive material (col. 4, lines 5-10). The sealing strips cover one octet strip of the plate, to define segments which can be used individually (col. 6, lines 27-40).

C) Cottingham does not teach 96 reaction chambers or different concentrations of aliquoted nucleic acids.

D) Regarding claims 12, 13, 16, 23, 27 and 28, Longiaru et al. teach preparation of microplates with capture probes for quantitation of amplification reaction products. The known amounts (25 ng) of probes are non-covalently bound to the wells of either a 96-well plate or to strips of 12 tubes which fit into strip holders in a microtiter plate format, and the plates are sealed (page 6, lines 26-46).

E) Longiaru et al. do not teach different concentrations of probes.

F) Irvine et al. teach quantitation of HIV DNA by amplification of sample containing the HIV DNA on a microplate, the wells of which contain known amounts of HIV DNA in the range of

10 to 200 tmoles (1 tmole = 602 molecules), and preparing standard curve of the DNA concentration (col. 13, lines 17-50).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used multiple reaction chambers, such as wells on a microplate of Longiaru et al., and multiple concentrations of nucleic acid of Irvine et al., in the method of formation of reaction chambers of Klatser et al. The motivation to do so, provided by Cottingham, would have been that multiple well format can be conveniently handled by clinical personnel and all reagents for both DNA amplification and detection are provided within the device (col. 2, lines 45-49, 55-61). The motivation to do so, provided by Irvine et al., would have been that having a set of standard nucleic acids provided means for determining the concentration of HIV DNA down to 50 tmoles (= about 30,000 molecules) (col. 14, lines 5-17).

14. Claims 5, 10, 21 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klatser et al. (J. Clin. Microbiol., vol. 36, pp. 1798-1800, June 1998), Koehler et al. (Biotechniques, vol. 23, pp. 722-726, 1997; cited in the IDS) and Barany et al. (U.S. patent No. 5,494,810).

A) Klatser et al. do not teach carrier nucleic acid being λ DNA.

B) Koehler et al. teach addition of λ DNA digested with HindIII as a carrier to stabilize standard DNA in solution (page 724, second paragraph; page 725, second paragraph). Koehler et al. do not teach sonicated λ DNA.

C) Barany et al. teach using sonicated salmon sperm DNA as a carrier (col. 34, lines 29, 30).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used λ DNA as a carrier in the formation of plates of Klatser et al. The motivation to do so, provided by Koehler et al., would have been that presence of carrier DNA stabilized DNA in dilute solution and prevented non-specific binding of DNA to the tubes (page

724, second paragraph) and diminished variability in the amplification reactions using the competitor in solution (page 725, second paragraph). The motivation to sonicate the λ DNA of Koehler et al., provided by Barany et al., would have been that the sonicated DNA provided no background in amplification reactions (col. 36, lines 21-23).

15. Claims 9 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klatser et al. (J. Clin. Microbiol., vol. 36, pp. 1798-1800, June 1998), Koehler et al. (Biotechniques, vol. 23, pp. 722-726, 1997; cited in the IDS) and Miyamura et al. (U.S. Patent No. 5,747,241).

A) Klatser et al. do not teach dilution of DNA standards using a DNA solution having a minimum sequence homology to the nucleic acid being analyzed, or dilution of RNA standards using tRNA solution.

B) Koehler et al. teach addition of λ DNA digested with HindIII as a carrier to stabilize standard DNA in solution (page 724, second paragraph; page 725, second paragraph). Koehler et al. do not teach using tRNA.

C) Miyamura et al. teach adding tRNA to a serum sample which contains HCV RNA (col. 2, lines 63-67; col. 3, lines 1-9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used λ DNA of Koehler et al. as a carrier in the formation of plates of Klatser et al. The motivation to do so, provided by Koehler et al., would have been that presence of carrier DNA stabilized DNA in dilute solution and prevented non-specific binding of DNA to the tubes (page 724, second paragraph) and diminished variability in the amplification reactions using the competitor in solution (page 725, second paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used tRNA of Miyamura et al. as a carrier in the formation of plates of Klatser et al. The motivation to do so, provided by Miyamura

et al., would have been that the presence of tRNA was advantageous because it provided an indicator of RNA degradation (col. 3, lines 4-9).

16. No claims are allowed.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TS
February 17, 2004

JEFFREY FREDMAN
PRIMARY EXAMINER